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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,114	02/09/2001	Tsutomu Nobori	02307O103031	8926

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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,114	NOBORI ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 12-22* is/are pending in the application.

4a) Of the above claim(s) *10 and 12-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1202* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed January 21, 2003. Currently, claims 10, 12-16, 17-22 are pending. Claims 10, 12-16 have been withdrawn as drawn to non-elected subject matter.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn in view of the amendments to the claims or applicant's remarks.

New Grounds of Rejection Necessitated by Amendment

New Matter

4. Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8" are included. The amendment proposes that the new claim language is supported by the specification at page 16, lines 10-22 and in the application filed December 1993. However, the specification does not describe or discuses "nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8". In

the application filed in December 1993, the specification states that the nucleic acid in Figure 1 is the gene. Therefore, there is no contemplation that these are exons 4-8. However, page 30 of the specification filed December 1993 provides Example VI to obtain the missing 5' end of cDNA of MTAse. Therefore, the specification also appears to indicate that the 5' portion of the cDNA is missing. The specification describes hybridization to detect cDNA clones derived from sources where extremely low amount of mRNA sequence relating to the polypeptide are present (page 16, lines 10-22). This description does not support nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8. The concept of "nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8" does not appear to be part of the originally filed invention. Therefore, "nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8" constitutes new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to "a nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8 which encodes MTAse."

The specification teaches a genomic sequence for the gene for MTAse and indicates the location of exons in the polynucleotide. The specification teaches "the preseumed exons are underline; presumed introns are indicated by one or more "N" substitutions for bases in the polynucleotide sequence." Example 1 teaches a test for MTAse Catalytic activity in a sample (page 23).

The instant claims are broadly drawn to encompass full length cDNA, introns, the MTAse gene including regulatory regions. The specification, as of the instant application, describes a nucleic acid sequence comprising 8 exons. The Figure contains several regions of "N." However, theses regions do not appear to be the exact length or contain any specific nucleotides of the actual introns of the gene. The claims are directed to hybridization language which is not directed to any particular stringency. The single example in the Written Description Guidelines, namely Example 9, is directed to high stringency conditions which are 6XSSC and 65 degrees Celsius. Moreover, the claim is drawn to a nucleic acid that hybridizes over the entire cDNA, as opposed to a single exon. The instant claims do not contain either high stringency

limitations or the limitations of hybridizing over the entire cDNA. Therefore, the claims encompass homologues, splice variants and additional nucleic acids which may contain a conserved domain over a small region of the nucleic acid. Therefore, unlike Example 9, there is no actual reduction to practice of the claimed invention, clear depiction of the claimed invention in the drawings or a complete detailed description of the structure. There is no known or disclosed correlation between the function of MTAse and the structure of the non-described regulatory elements and untranslated regions of the gene. There is no additional disclosure of physical and/or chemical properties. Weighing all factors in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid consisting of SEQ ID NO: 1, does not reasonably provide enablement for a nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8 which encodes MTAse. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to "a nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from the group consisting of exon 4-8 which encodes MTAse."

The specification teaches a genomic sequence for the gene for MTAse and indicates the location of exons in the polynucleotide. The specification teaches "the preseumed exons are underline; presumed introns are indicated by one or more "N" substitutions for bases in the polynucleotide sequence." Example 1 teaches a test for MTAse Catalytic activity in a sample (page 23).

At the time of the date or priority for the instant claims, namely 3/26/1997, the art has not described introns or regulatory regions of the MTAse (i.e. MTAP gene).

Neither the specification nor the art teach the skilled artisan how to use the invention as broadly as claimed. The instant claims are broadly drawn to encompass

full length cDNA, introns, the MTAse gene including regulatory regions. The specification, as of the instant application, teaches a single nucleic acid sequence comprising 8 exons. The Figure contains several regions of "N." However, theses regions do not appear to be the exact length or contain any specific nucleotides of the actual introns of the gene. The claims are directed to hybridization language which is not directed to any particular stringency. Therefore, the claims encompass homologues, splice variants and additional nucleic acids which may contain a conserved domain over a small region of the nucleic acid. While one could conduct additional experimentation to determine the nucleic acid sequence of the gene, the regulatory regions, homologues, splice variants and the introns, the outcome of such research cannot be predicted, and such further research and experimentation are both unpredictable and undue. It is unpredictable which nucleic acids which hybridize to a single exon would encode a MTAse. The skilled artisan would be required to perform additional experimentation to determine whether each nucleic acid which hybridized would enode a MTAse. It is unpredictable which nucleic acids would encode MTAse prior to the additional experimentation.

Maintained Rejections

Priority

5. This application claims priority to 09/072,914, 08/827,342, 08/459,343, 08/176,855.

With respect to Claim 17-22, the Claim is awarded priority to the filing date of 3/26/97 for the invention of a nucleic acid sequence having SEQ ID NO: 1 which encodes the MTAse. The 08/459,343 application, filed 6/2/95, which is a divisional of 08/176,855. disclosed SEQ ID NO: 1 containing a partial genomic sequence of the MTAse gene and therefore did not encode MTAse (since it did not contain all of the sequences indicated as coding sequences in Figure 1 and SEQ ID NO: 1 of the present application).

Response to Arguments

The response traverses the date or priority. The response asserts that the priority will be extended back to the earliest related application, namely December 1993. This argument has been reviewed but is not convincing because Claim 17 is directed to an isolated polynucleotide which encodes MTAse comprising a nucleotide sequence that hybridizes under stringent conditions to an exon of SEQ ID NO: 1, wherein the exon is selected from exon 4-8 shown in Figure 1. The claim reads on the full length cDNA and the gene which encompasses introns and regulatory regions. In December 1993, Figure 1 of the specification only contains 5 regions of underlining. The instant specification asserts that there are 8 exons. Moreover, when comparing the sequence to the instant sequence, the first three exons, namely approximately 800 nucleotides are

missing. Additionally, the sequences contain regions of "N" which denote "presumed introns." Thus, at the time of December 1993, the specification did not disclose the full scope of the invention encompassed by the instant claims. Moreover, Exon 4 of the instant application contains a different boundaries than the Figure in December 1993. For example the Figure in the instant application begins exon 4 with a GC and ends with an AG, whereas the Figure 1 in 1993 begins with an AG and ends an AC. Exon 5 also contains different boundaries. Moreover, the string of N's are in different locations in each of the figures. Therefore, the instant claims receive benefit to March 26, 1997.

Thus for the reasons above and those already of record, the date of priority is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily

published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 17-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Olopade et al (PNAS Vol. 92, pages 6489-6493, July 1995).

It is noted that since the priority of Claim 11 is 3/26/97, the instant rejection is applicable.

Olopade et al teaches the cloning of the cDNA of the methylthioadenosine phosphorylase gene which encodes the methyladenosine phosphorylase protein (see Figure 3, page 6492) (MTAP and MTAse are the same protein). CDNAs were taught as having been cloned into lambda gt 10 or gt11 (lambda gt 11 is an expression vector) and subcloned into bluescript (also an expression vector) for sequencing (see page 6490, col. 2). The sequence of Olapade is interpreted as being substantially similar to the sequence contained in SEQ ID NO: 1 and the expression vectors taught by Olopade are interpreted as containing pepetide encoding fragments of the polynucleotide of Claim 7 (the fragments in this case are the exons). Olopade et al also teaches YAC clones, A73B12 and 802B11 which include the MTAP gene and therefore, inherently hybridize under stringent conditions to an exon of SEQ ID NO: 1 and inherently encode MTAse.

Response to Arguments

The response traverses the rejection. The response asserts that Olopade was not published before the earliest priority date of the claimed invention. This argument has been reviewed but is not convincing because, while Olopade is published after

1993, Olopade is published before the instant priority date of the instant claims. The nucleotide sequence of the MTAP cDNA is provided in Figure 3A. Therefore, the cDNA of Olopade hybridizes to a cDNA nucleic acid comprising exon 4-8. Thus for the reasons above and those already of record, the rejection is maintained.

7. Claims 17-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Nobori et al (PNAS Vol. 93, pages 6203-6208, June 1996).

Nobori et al. (herein referred to as Nobori) teaches subcloning DNA from phage and cosmid clones into pBluescript, an expression vector (page 6204) (cDNA and genomic cloning of MTAP gene). Figure 2 of Nobori teaches the DNA sequences of the protein-coding exons and their flanking regions in the human MTAP gene (page 6205). The nucleic acid shown in Figure 2 contains exons 1-8 which will hybridize under stringent conditions to an exon of SEQ ID NO: 1. Therefore, Nobori anticipates the claimed invention.

Response to Arguments

The response traverses the rejection. The response asserts that Nobori was published in June 1996 which is after the priority date. This argument has been reviewed but is not convincing because the priority date awarded to the instant claims is 3/26/1997. For the reasons discussed above, the instant claims are not supported in the earliest filing date. Therefore, the nucleic acid of Nobori anticipates the claimed invention. Thus for the reasons above and those already of record, the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 17-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7, 9 of U.S. Patent No. 5,942,393, August 24, 1999. Although the conflicting claims are not identical, they are not patentably distinct from each other because the sequence recited in Claim 7, 9 of the '113 application, having the nucleotide sequence shown in SEQ ID NO: 1, or comprising only the exon coding regions of the nucleic acid sequence of Figure 1 would hybridize under stringent conditions to an exon of SEQ ID NO: 1.

Response to Arguments

The response traverses the rejection. The response asserts that Claim 11 has been cancelled and therefore the rejection is moot. This argument has been reviewed but is not convincing because the claim still are not patentably distinct from each other because the instant claims are generic to the patented claims. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

9. No claims allowable over the art.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
May 19, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
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